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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,894	07/17/2003	Georg Watzek	35931-PCT-USA-A 071986.02	1493

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,894	WATZEK ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/07/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/07/2006 has been entered.

Claims 1-10 and 13 as amended (12/07/2006) are under examination in the instant office action.

Applicants canceled claims 11, 12 and 14-16.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application A 89/2001 filed in Austria on 1/18/2001.

It is noted, however, that a certified copy of this application as required by 35 U.S.C. 119(b) is missing in the instant IFW application.

Please, provide a copy of the priority document for scanning.

Claim Rejections - 35 USC § 112

Claims 2-10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 are uncertain and indefinite for failure of further limit the claimed drug composition. It is unclear as claimed whether the recited materials and/or compounds are

structural constituents of "microparticles" or whether they are additional materials that are "further" included in the drug composition. In the office action the recited materials are interpreted as additional components. It is suggested to insert phrase "further" in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,165,938 (Kinghton) as explained in the prior office action and repeated herein.

Claims are directed to a drug composition for topical application as intended for wound healing wherein the composition comprises microparticles from activated blood cells, wherein composition has been made under sterile conditions and subjected to virus inactivation and/or depletion and wherein composition is in a freeze-dried or deep-frozen state. Some claims are further drawn to the presence of growth factors or substances promoting wound healing in the drug composition. Some claims are further drawn to the presence of matrix materials, collagen, fibrinogen, thrombin and/or organic polymers and inorganic compounds in the drug composition. Some claims are further drawn to incorporation of biocompatible materials into the drug composition.

US 5,165,938 (Kinghton) discloses a drug composition produced from blood and intended for topical application and wound healing (abstract). The drug composition contains

"microparticles" derived from platelet-rich plasma after activation and centrifugation. The "microparticles" are mixed with microcrystalline collagens and frozen (col. 2, lines 20-55 or col.3, lines 25-44). The drug composition is made under sterile condition (col.3, line 26). Blood is collected from normal patients that are not diagnosed with viral diseases and, thus, virus depleted or virus free. The cited patent discloses that drug composition contains growth factors PDAF and PDGF or substances promoting wound healing. Fibrinogen and thrombin are inherent components of a product derived from platelet rich plasma. Proteins and/or glycoproteins of platelet rich plasma fall within the meaning of generic organic polymers as claimed. The drug composition contains inorganic compounds or inorganic salts (col. 3, line 42). The cited patent teaches the use of composition in conjunction with biodegradable dressings and implantable devices (col. 4, lines 32-35).

Thus, the cited patent anticipates the claimed invention.

Claims 1-4 and 6-9 remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,185,160 (Chao) as explained in the prior office action and repeated herein.

Claims are directed to a drug composition for topical application as intended for wound healing wherein the composition comprises microparticles from activated blood cells, wherein composition has been made under sterile conditions and subjected to virus inactivation and/or depletion and wherein composition is in a freeze-dried or deep-frozen state. Some claims are further drawn to the presence of growth factors or substances promoting wound healing in the drug composition. Some claims are further drawn to the presence of matrix materials, fibrinogen,

thrombin and/or organic polymers and inorganic compounds in the drug composition. Some claims are further drawn to incorporation of biocompatible materials into the drug

US 5,185,160 (Chao) discloses a pharmaceutical composition comprising viral-inactivated blood platelet membrane microparticles (abstract). Microparticles are derived from platelet poor plasma and separated by sequential centrifugations (col. 4, lines 1-60); virus inactivation is made by heat treatment (abstract and col. 4, lines 40-45); drug composition is provided in frozen or lyophilized (freeze-dried) state (col.4, lines 60-62); the drug composition is made under sterile conditions (col. 3, line 63). The drug composition comprises physiological saline (col. 4, line 41) and, thus, inorganic compounds. Fibrinogen and thrombin are inherent components of a product derived from plasma, particularly in view that the cited patent discloses that microparticles fractions retains "procoagulant" activity (col. 5, lines 64-67). Proteins and/or glycoproteins (GPIb, for example: col. 5, line 11) in the final preparation as disclosed fall within the meaning of generic organic polymers as claimed. Although the particular application of the cited product relates to transfusion as intended to reduce bleeding time, the bleeding reducing drug would clearly be suitable in wound healing. The differences between drug composition as intended for transfusion and as intended for topical application would relate to carriers (inactive ingredient) or to dosage of active ingredient. The claimed invention is not so limited.

Thus, the cited patent anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 and 13 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,165,938 (Kinghton) and US 5,185,160 (Chao) taken with US 5,697,980 (Otani et al.).

Claims are directed to a drug composition for topical application as intended for wound healing wherein the composition comprises microparticles from activated blood cells, wherein composition has been made under sterile conditions and subjected to virus inactivation and/or depletion and wherein composition is in a freeze-dried or deep-frozen state. Some claims are further drawn to the presence of growth factors or substances promoting wound healing in the drug composition. Some claims are further drawn to the presence of matrix materials, collagen, fibrinogen, thrombin and/or organic polymers and inorganic compounds in the drug composition. Some claims are further drawn to incorporation of biocompatible materials into the drug composition. Some claims are further drawn to biocompatible materials or carriers such as titanium, apatite and organic polymer polyactone.

US 5,165,938 (Kinghton) and US 5,185,160 (Chao) are relied upon as explained above for the disclosure of drug comprising microparticles derived from activated blood cells or platelets that are separated by centrifugation, subjected to viral inactivation, made under sterile conditions and provided in frozen and freeze-dried state. The cited drug compositions are intended for wound healing and reduction of bleeding. The cited drug compositions comprise carriers including collagen and saline as intended for particular mode of administration. US 5,165,938 (Kinghton) suggest incorporation of microparticles derived from blood platelets into

dressing materials and as coating over implantable devices. But the cited patents are missing particular disclosure about the use of titanium, apatite and organic polymers as material for carriers and/or medical devices.

However, US 5,697,980 (Otani et al.) teaches artificial filling and prosthetic device(s) capable of adhering to tissues or to wounded tissues. The materials include titanium core coated with calcium phosphate (apatite) and organic polymers including polycaprolactone or polyactone. For example: see abstract; col. 2, line 26 and lines 37-40; col. 3, lines 33-45 and col. 4, lines 10-17).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to add various carriers, fillings, biodegradable materials and devices including titanium, apatite and organic polymers to modify the drug compositions taught by US 5,165,938 (Kinghton) and/or US 5,185,160 (Chao) as suggested by US 5,165,938 (Kinghton) with a reasonable expectation of success in wound healing because the claimed carriers and materials are known and used for making artificial filling, carriers and medical devices as adequately demonstrated by US 5,697,980 (Otani et al.). One of skill in the art would have been motivated to adjust carrier compositions of US 5,165,938 (Kinghton) and of US 5,185,160 (Chao) with regard to a mode of administration for the expected benefits in wound healing and/or in bleeding reduction as provided by microparticles derived from blood platelets.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 12/07/2006 have been fully considered but they are not persuasive.

1. With respect to the claims rejected under 35 U.S.C. 102(b) as being anticipated by US 5,165,938 (Kinghton) applicants' main argument is directed to the idea that the cited drug preparation is not necessarily virus-free since the cited patent does not explicitly describe an active step of viral decontamination or viral deactivation (response pages 6-7). This argument is not found persuasive because claim limitation drawn to a procedure of virus inactivation relates to a product-made-by-process. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. MPEP 2113. The final structure of the presently claimed product encompasses a sterile drug product that would be free of viruses. The drug composition of the cited US 5,165,938 (Kinghton) is made under sterile condition (col. 3, line 26) and blood materials are derived from normal patients that are not diagnosed with viral diseases and, thus, starting materials and final preparations are virus free. Applicants appear to argue that the cited patent acknowledges potential contamination with hepatitis. However, US 5,165,938 (Kinghton) teaches that starting materials that might have potential contamination with hepatitis are avoided (col. 4, lines 50-63). Thus, the drug composition of the cited US 5,165,938 (Kinghton) is reasonably expected to be free of viruses and, thus, it has the same structure as implied by the steps recited in the presently claimed product-made-by-process.

2. With regard to the claim rejected under 35 U.S.C. 102(b) as being anticipated by US 5,185,160 (Chao) applicants main argument is directed to the idea that although Chao's patent

refers to "microparticles", these "microparticles" are not the same as the "microparticles" of the present invention because the starting platelets utilized in the Chao's method were not activated (response paragraph bridging pages 8 and 9). This argument is not found particularly convincing because the Choa's "microparticles" are platelet membrane microvesicles (see title) that are obtained by freeze thawing of platelets. It is known that the blood platelets are activated by freeze thawing as evidenced by Exner et al. (Blood Coagulation and Fibrinolysis. December 2003), Vol.14, No. 8, pages 773-779), for example: see abstract.

The references cited by applicants in the response papers (pages 7-8) has been fully reviewed. Applicants appear to argue that the microparticles are the product of a controlled shedding process upon platelet activation by various agents or conditions. Yet, the claimed invention neither indicate the mode of platelet activation and/or of microparticles shedding from platelet membranes, nor there is any support in the as-filed specification to establish some structural differences between microparticles obtained by activation as disclosed the cited prior art and by activation means as intended by applicants.

Accordingly to Horstman's definitions (IDS reference) microparticles are membrane vesicles or membrane fractions released by platelets during activation and they have procoagulant activity and PF3 activity (see page 113, col.1, par. 1 and par. 3). The Chao's patent teaches exactly the same preparation of platelet-derived microparticles as defined by Horstman (IDS reference) that are platelet membrane microparticle fractions (col. 2, lines 26-27), that have procoagulant activity (col. 2, line 38) and they have PF3 activity (col. 3, line 18). Thus, the microparticles of Chao have the same structure or the same "moieties" as the applicants' claimed

microparticles and they have the same activity as the applicants' microparticles as argued, as defined in the as-field specification and in the light of the prior art definitions.

3. With regard to claim rejection under 35 USC § 103 applicants argue that there is no suggestion and/or motivation to combine the cited references and that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (response pages 10-12).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, both US 5,165,938 (Kinghton) and US 5,185,160 (Chao) teach drug compositions comprising blood cell derived microparticles that are intended for wound healing and shortening of bleeding time, and, thus, suitable for tissue regeneration within the meaning of the instant

claims. The pharmaceutical and/or therapeutic compositions commonly contains active ingredients together with carriers. Thus, addition to the drug compositions of matrix carriers and/or adjuvants known and available in the prior art as adequately demonstrated by US 5,697,980 (Otani et al.) is considered to be obvious in the absence of evidence to the contrary.

Claim rejection over reference by Zeng (The Southeast Asian Journal of Tropical Medicine and Public Health. 1993. Vol. 24, Suppl. 1, pages 204-205) has been withdrawn as result of correction of typing error in term "polyactone".

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova, AU 1657

February 27, 2007

V. Afremova

VERA AFREMOVA

PRIMARY EXAMINER